

In the Specification

On page 1, kindly replace the first and second paragraphs with the following:

RELATED APPLICATION

This is a continuation of International Application No. PCT/JP2004/017666, with an international filing date of November 22, 2004 (WO 2005/073155 A1, published August 11, 2005), which is based on Japanese Patent Application No. 2004-020166, filed January 28, 2004.

TECHNICAL FIELD

~~The present invention~~This disclosure relates to a method for producing an aldehyde compound or a ketone compound using a microreactor. ~~More, particularly, the present invention relates to a method for producing an aldehyde or ketone compound from a primary or secondary alcohol and through the Swern oxidation reaction using a microreactor.~~

~~BACKGROUND-ART~~

When the Swern oxidation reaction is used to produce an aldehyde compound or a ketone compound from a primary or secondary alcohol, no waste containing a heavy metal is produced and the reaction can be widely applied to various compounds. Also no excess oxidation arises and epimerization, at the α -position with respect to a carbonyl group, does not arise. Therefore, this method is widely used as an organic synthesis reaction method.

Kindly replace the paragraph spanning pages 1 and 2 with the following:

As a trial using a microreactor for an organic chemical reaction, for example, Japanese Unexamined Patent Publication (Kokai) No. 2002-155007 (~~Patent Document 1~~) discloses that a fine-structured reaction system is used so as to produce aldols from aldehydes and/or ketones at a temperature of -10 to +250°C through a catalytic reaction, while Japanese Unexamined Patent Publication (Kokai) No. 2003-113185 (~~Patent Document 2~~) discloses a method, for producing an

allylboron compound and an alkylboron compound, which comprises reacting a lithium aromatic and an aliphatic compound with a boron compound at a temperature of -60°C to +30°C using a microreactor.

On page 2, kindly replace the first and second full paragraphs with the following:

Furthermore, Kohyo (National Publication of Translated Version) No. 2003-506339 (~~Patent Document 3~~) discloses a method for a Friedel-Crafts acylation reaction of an acylating agent and strong acid with an organic compound (preferably, an aromatic or heteroaromatic compound) in a microreactor at a temperature of 10 to 90°C. Furthermore, Japanese Unexamined Patent Publication (Kokai) No. 2003-128677 (~~Patent Document 4~~) discloses a method, for producing an allylboron and an alkylboron, which comprises reacting a halide of allylmagnesium and alkylmagnesium with a boron compound in a microreactor at a temperature of -60°C to +80°C.

However, there has never been known a method capable of industrially carrying out the Swern reaction of a primary or secondary alcohol using a microreactor.

~~[Patent Document 1] Japanese Unexamined Patent Publication (Kokai) No. 2002-155007~~

~~[Patent Document 2] Japanese Unexamined Patent Publication (Kokai) No. 2003-113185~~

~~[Patent Document 3] Japanese Unexamined Patent Publication (Kohyo) (National Publication of Translated Version) No. 2003-506339~~

~~[Patent Document 4] Japanese Unexamined Patent Publication (Kokai) No. 2003-128677~~

On page 3, kindly replace the first through third paragraphs with the following:

DISCLOSURE OF THE INVENTION SUMMARY

~~An object of the present invention is to~~ We provide a methods for producing an aldehyde compound or a ketone compound from a primary or secondary alcohol at a higher temperature than that in case of a conventional method, within a short time and with a high yield.

~~The above object can be achieved by the method of the present invention.~~

~~The method of the present invention,~~ for producing an aldehyde compound or a ketone compound using a microreactor, comprises a step (1) of mixing a liquid containing a sulfoxide compound with a liquid containing an activating agent for the sulfoxide compound to allow them to react with each other and to produce an activation reaction product of the sulfoxide compound; a step (2) of mixing the liquid containing the activation reaction product of the sulfoxide compound with a liquid containing at least one member selected from primary and secondary alcohols to allow them to react to each other and to prepare a liquid containing an alkoxysulfonium salt; and a step (3) of mixing the resulting liquid containing an alkoxysulfonium salt with a basic compound-containing liquid and to allow them to react with each other and to prepare a liquid containing an aldehyde compound or a ketone compound corresponding to the alkyl alcohol, wherein at least one step of the steps (1), (2) and (3) is carried out using a microreactor.

Kindly replace the paragraph spanning pages 3 and 4 with the following:

~~In the method of the present invention, the~~The microreactor preferably comprises two liquid-introducing channels having a fine cross-sectional profile for introducing two type of liquids; one micromixer portion, for mixing and reacting the two kinds of introduced liquids with each other, having a fine cross-sectional profile and connected to the liquid introducing channel; and one liquid discharging channel for discharging a reaction product liquid from the micromixer portion, having a fine cross-sectional profile.

On page 4, kindly replace the first through seventh full paragraphs with the following:

~~In the method of the present invention, preferably~~Preferably, two steps connected to each other are carried out by using a microreactor and a liquid discharging channel of a reactor of an upstream step and a liquid introducing channel of a reactor of a downstream step connected to the

upstream step, are connected with each other through a connecting capillary tube.

~~In the method of the present invention, the~~The steps (1) and (2) are preferably carried out in the microreactor.

~~In the method of the present invention, the~~The temperatures of the liquids in the micromixer portion and the liquid discharging channel of the microreactor are preferably adjusted to a desired values.

~~In the method of the present invention, the~~The temperature of the liquids in the connecting capillary tube is preferably adjusted to a desired value.

~~In the method of the present invention, preferably~~Preferably, the cross-sectional area of the liquid introducing channel, that of the liquid micromixer portion and that of the liquid discharging channel in the microreactor, are respectively $0.7 \mu\text{m}^2$ to 1 mm^2 , $0.7 \mu\text{m}^2$ to 1 mm^2 and $0.7 \mu\text{m}^2$ to 1 mm^2 .

~~In the method of the present invention, a~~A major diameter/minor diameter ratio of the cross section of the liquid introducing channel, the liquid micromixer portion and the liquid discharging channel in the microreactor, is preferably 1 or more and the minor diameter is preferably within a range from $1 \mu\text{m}$ to 1 mm .

~~In the method of the present invention, preferably~~Preferably, in the microreactor, the flow rate of the liquid to be discharged from the liquid micromixer is adjusted so that two kinds of liquids mixed with each other can be reacted to each other in the microreactor with a desired mixing efficiency and a desired retention time.

On page 5, kindly replace the first through seventh paragraphs with the following:

~~In the method of the present invention, the~~The residence time of the liquid in the microreactor is preferably adjusted within a range from 0.001 to 60 seconds.

~~In the method of the present invention, preferably~~Preferably, step (1) is carried out using a microreactor and the residence time of a mixed reaction solution of the sulfoxide compound-containing liquid with an activating agent-containing liquid in a portion of the microreactor between the inlet of the micromixer portion and the inlet of the reactor for the step (2) is in the range of from 0.001 to 60 seconds.

~~In the method of the present invention, preferably~~Preferably, step (1) is carried out in the microreactor and the reaction temperature in step (1) is in the range of from -80 to +50°C, more preferably from -30 to +40°C.

~~In the method of the present invention, preferably~~Preferably, the step (2) is carried out in the microreactor and the mixing reaction temperature in the step (2) is in the range of from -80 to +50°C, more preferably from -30 to +40°C.

~~In the method of the present invention, the~~The sulfoxide compound is preferably selected from a dialkyl sulfoxide.

~~In the method of the present invention, dimethyl~~Dimethyl sulfoxide is preferably used as a dialkyl sulfoxide.

~~In the method of the present invention, the~~The activating agent for a sulfoxide compound is preferably selected from acetic anhydride, oxalyl chloride, trifluoroacetic anhydride, trifluoromethanesulfonic anhydride, diphosphorus pentaoxide, chlorine, benzoyl chloride, acetyl chloride, methanesulfonyl chloride, p-toluenesulfonyl chloride, sulfur trioxide-pyridine complex and 2,4,6-trichloro-1,3,5-triazine.

Kindly replace the paragraph spanning pages 5 and 6 with the following:

~~In the method of the present invention, the~~The primary and secondary alcohols are preferably selected from saturated and unsaturated C₁-C₂₀ aliphatic primary and secondary alcohols, or saturated

and unsaturated aliphatic primary and secondary alcohols having an alicyclic aromatic hydrocarbon group, and saturated and unsaturated primary and secondary alcohols having a heterocyclic group.

On page 6, please replace the first through sixth full paragraphs with the following:

~~In the method of the present invention, the~~The basic compound is preferably selected from organic amine compounds.

~~In the method of the present invention, the~~The organic amine compound is preferably selected from trialkylamines.

~~In the method of the present invention, a~~A molar ratio of the sulfoxide compound to be supplied to the first step to the primary or secondary alcohol to be supplied to the second step is preferably within a range of from 1:1 to 20:1.

~~In the method of the present invention, a~~A molar ratio of the activating agent for a sulfoxide compound to be supplied to the first step to the primary or secondary alcohol to be supplied to the second step is preferably within a range of from 1:1 to 2:1.

~~In the method of the present invention, a~~A molar amount of the base compound to be supplied to the third step is preferably 2 to 20 times the molar amount of the primary or secondary alcohol to be supplied to the second step.

~~The methods of the present invention~~ may further comprise a step of isolating the target aldehyde or ketone compound from the aldehyde or ketone compound-containing liquid prepared in the step (3).

Kindly replace the paragraph spanning pages 6 and 7 with the following:

When an aldehyde compound or a ketone compound is produced from a corresponding primary or secondary alcohol ~~in accordance with the method of the present invention~~, the use of a microreactor in at least one step of the method enables a relatively high temperature of, for example,

about 20°C to use in place of a low temperature of -50°C used in the conventional method, and the target compound to be produced at a high yield within a short time.

On page 7, kindly replace the first full paragraph with the following:

~~BEST MODE FOR CARRYING OUT THE INVENTION~~DETAILED DESCRIPTION

The method for producing a corresponding aldehyde compound or a corresponding ketone compound by using a microreactor comprises:

a step (1) of mixing a liquid containing a sulfoxide compound with a liquid containing an activating agent for the sulfoxide compound to allow them to react with each other and to produce an activation reaction product of the sulfoxide compound;

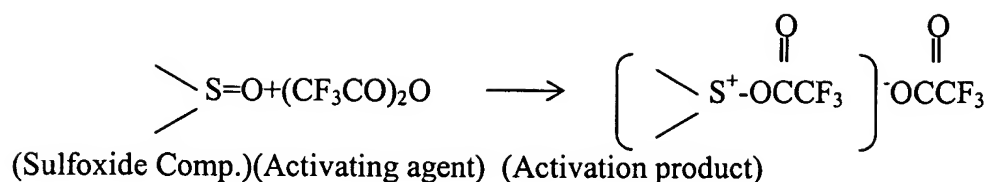
a step (2) of mixing the liquid containing the activation reaction product of the sulfoxide compound with a liquid containing at least one member selected from primary and secondary alcohols to allow them to react with each other and to prepare a liquid containing an alkoxysulfonium salt; and

a step (3) of mixing the resulting liquid containing an alkoxysulfonium salt with a basic compound-containing liquid to allow them to react with each other and to prepare a liquid containing an aldehyde compound or a ketone compound corresponding to the alkyl alcohol, wherein at least one step of the steps (1), (2) and (3) is carried out by using a microreactor.

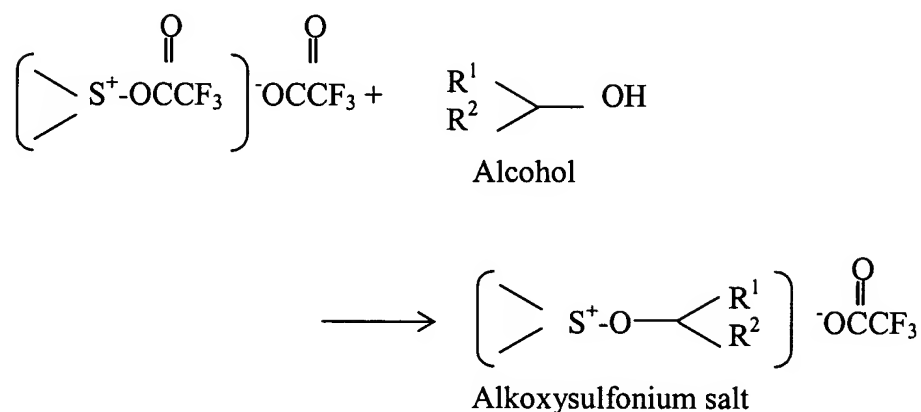
Kindly replace the paragraph spanning pages 7 and 8 with the following:

The steps (1), (2) and (3) ~~of the method of the present invention~~ are carried out according to the following reaction scheme (1):

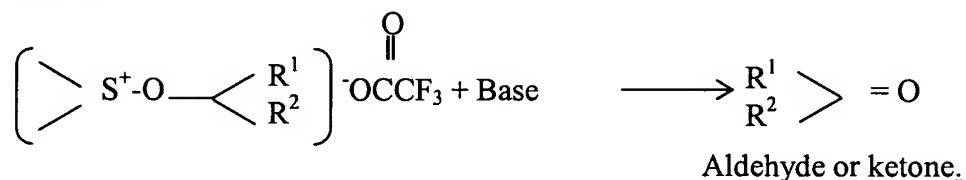
Step (1)



Step (2)



Step (3)



On page 9, kindly replace the second and third full paragraphs with the following:

In the method of the present invention, in the case where two steps connected to each other are carried out by using microreactors, a liquid-discharging channel of a reactor of the upstream step and a liquid-discharging channel of a reactor of the downstream step are preferably connected with each other through a connecting capillary tube. The temperature of the liquid mixture obtained by uniform mixing in the micromixer can be adjusted to a desired temperature in the micromixer and the liquid-discharging channel and also the desired reaction can be allowed to proceed and complete.

The connecting capillary tube is preferably provided with means for adjusting the temperature of the liquid which flows through the connecting capillary tube. The means may be a constant temperature bath, a temperature control jacket or the like.

~~In the method of the present invention, as described above,~~ As described above, the microreactor is preferably used in at least the two steps (1) and (2). Thereby, main reaction steps (1) and (2) ~~of the method of the present invention~~ can be accurately controlled and the respective reactions can be completed within a reduced time and with high efficiency.

Kindly replace the paragraph spanning pages 9 and 10 with the following:

In the microreactor ~~used in the method of the present invention~~, the areas of the cross-sections of the liquid-introducing channel, the liquid micromixer portion and the liquid-discharging channel are respectively and preferably from $0.7 \mu\text{m}^2$ to 1 mm^2 (more preferably from 0.007 to 0.7 mm^2), $0.7 \mu\text{m}^2$ to 1 mm^2 (more preferably from 0.007 to 0.7 mm^2) and $0.7 \mu\text{m}^2$ to 1 mm^2 (more preferably from 0.007 to 0.7 mm^2), and the major diameter/minor diameter ratios of the cross sections are preferably 1 or more and the minor diameters of the cross-sections are preferably within a range from $1 \mu\text{m}$ to 1 mm , and more preferably from 25 to $500 \mu\text{m}$.

On page 10, kindly replace the first through third full paragraphs with the following:

In the microreactor ~~used in the method of the present invention~~, the flow rate of the liquid to be discharged from the liquid micromixer is defined so as to react two kinds of liquids mixed in the microreactor with a desired mixing efficiency and a desired residence time.

~~In the method of the present invention, each~~ Each reaction time in the reactions (1), (2) and (3) can be appropriately adjusted, but the residence time of the liquid in the microreactor is preferably adjusted to within a range of from 0.001 to 60 seconds. ~~In the method of the present invention, the~~ The step (1) is preferably carried out in the microreactor and the mixing reaction

temperature is preferably from -30 to +50°C, and also the step (2) is preferably carried out in the microreactor and the mixing reaction temperature is preferably from -80 to +50°C, and more preferably from -30 to +40°C.

~~In the method of the present invention,~~ in case of the step of using no microreactor, a reactor comprising two liquid supply means and one product liquid discharging means, for example, a T joint type reactor can be used. The reactor is preferably provided with temperature-adjusting means, liquid flow rate-adjusting means, etc.

Kindly replace the paragraph spanning pages 10 and 11 with the following:

The sulfoxide compound to be supplied to the step (1) ~~of the method of the present invention~~ is preferably selected from a dialkyl sulfoxide and, more preferably, dimethyl sulfoxide is used. As the liquid containing a sulfoxide compound, an organic solvent solution of the sulfoxide compound is usually used. If the sulfoxide compound is liquid, it can be used as it is.

On page 11, kindly replace the third full paragraph with the following:

The activating agent for a sulfoxide compound to be used in the step (1) of the method ~~of the present invention~~ is preferably selected from acetic anhydride, oxalyl chloride, trifluoroacetic anhydride, trifluoromethanesulfonic anhydride, diphosphorus pentoxide, chlorine, benzoyl chloride, acetyl chloride, methanesulfonyl chloride, p-toluenesulfonyl chloride, sulfur trioxide-pyridine complex and 2,4,6-trichloro-1,3,5-triazin and, more preferably, trifluoroacetic anhydride and oxalyl chloride are used. The activating agent-containing liquid can be prepared by dissolving an activating agent in an organic solvent. This organic solvent is preferably the same as the organic solvent for a sulfoxide compound. The concentration of the activating agent in the activating agent-containing liquid is preferably from 0.1 to 15 mol/liter.

Kindly replace the paragraph spanning pages 11 and 12 with the following:

In the step (1) of the method ~~of the present invention~~, as shown in the step (1) of the reaction scheme (1), a sulfoxide compound is reacted with an activating agent (for example, trifluoroacetic anhydride) to produce an activation reaction product of the sulfoxide compound. The activation reaction product produced in the step (1) is unstable and exhibits the following tendency. Namely, at the temperature of -30°C or higher, Pummerer rearrangement occurs on the activation reaction product to cause the activation reaction product to be decomposed into $\text{CH}_3\text{S}^+ = \text{CH}_2$ and $\text{CF}_3\text{CO}_2\text{H}$ and, furthermore decomposition products to produce $\text{CH}_3\text{SCH}_2\text{OC(O)CF}_3$, or in the step (2), the decomposition reaction product reacts with a primary or secondary alcohol to produce $\text{R}^1(\text{R}^2)\text{-OCH}_2\text{SCH}_3$ (MTM ether), and in the step (3), $\text{CH}_3\text{SCH}_2\text{OC(O)CF}_3$ reacts with a base to produce $\text{R}^1(\text{R}^2)\text{-OC(O)CF}_3$ (TFA ester). When the reaction in the step (1) is completed by vigorous mixing using a microreactor and accurately control at a predetermined temperature, it becomes possible to prevent or reduce the Pummerer rearrangement and to feed an activation reaction product-containing liquid into the step (2).

On page 12, please replace the first full paragraph with the following:

In step (2) of the method ~~of the present invention~~, the activation reaction product-containing liquid introduced from the step (1) and a liquid containing at least one of primary and secondary alcohols are mixed and reacted to prepare a liquid containing an alkoxysulfonium salt shown in the step (2) of the reaction scheme (1).

Kindly replace the paragraph spanning pages 12 through 15 with the following:

The primary and secondary alcohols to be used in the step (2) of the method ~~of the present invention~~ are not noticeably limited as far as they are a primary alcohol and a secondary alcohol (which have an OH group combined with carbon atoms of an aliphatic hydrocarbon group but not

with carbon atoms constituting an aromatic ring (namely not a phenolic OH group)). The primary and secondary alcohols include the followings:

(1) C_1 - C_{20} Saturated and unsaturated aliphatic primary alcohols, for example, methyl alcohol, ethyl alcohol, n-propyl alcohol, butyl alcohol, isobutyl alcohol, pentyl alcohol, isopentyl alcohol, neopentyl alcohol, hexyl alcohol, isohexyl alcohol, heptyl alcohol, octyl alcohol, 2-ethylhexyl alcohol, nonyl alcohol, decyl alcohol, allyl alcohol, crotyl alcohol, propargyl alcohol, geraniol and phytol;

(2) alicyclic primary alcohols in which an -OH group is combined with carbon atoms of a C_1 - C_{12} alicyclic hydrocarbon ring via a linear hydrocarbon group having one or more carbon atoms, for example, cyclohexylmethyl alcohol, 2-norbornane methanol and 5-norbornene-2-methanol;

(3) aromatic primary alcohols in which an -OH group is combined with carbon atoms of an aromatic hydrocarbon ring via an alicyclic hydrocarbon group having one or more carbon atoms, for example, benzyl alcohol, phenethyl alcohol, cinnamyl alcohol, salicyl alcohol and 2-phenyl ethanol;

(4) heterocyclic primary alcohols in which an -OH group is combined with carbon atoms of a heterocyclic group via a C_1 linear hydrocarbon group having one or more carbon atoms, for example, furfuryl alcohol;

(5) C_3 - C_{20} saturated and unsaturated aliphatic secondary alcohols, for example, 2-propanol, 2-butanol, 2-pentanol, 3-pentanol, 2-hexanol, 3-hexanol, 2-heptanol, 3-heptanol, 4-heptanol, 2-octanol, 3-octanol, 4-octanol, 2-nonanol, 3-nonanol, 4-nonanol and 5-nonanol;

(6) C_3 - C_{20} alicyclic secondary alcohols, for example, cyclopentanol, 2-methylcyclopentanol, 3-methylcyclopentanol, 2-ethylcyclopentanol, 3-ethylcyclopentanol, 2-n-propylcyclopentanol, 3-n-propylcyclopentanol, 2-isopropylcyclopentanol, 3-isopropylcyclopentanol,

2-n-butylcyclopentanol, 3-n-butylcyclopentanol, 2-isobutylcyclopentanol, 3-isobutylcyclopentanol, 2-sec-butylcyclopentanol, 3-sec-butylcyclopentanol, 2-tert-butylcyclopentanol, 3-tert-butylcyclopentanol; cyclohexanol, 2-methylcyclohexanol, 3-methylcyclohexanol, 4-methylcyclohexanol, 2-ethylcyclohexanol, 3-ethylcyclohexanol, 4-ethylcyclohexanol, 2-n-propylcyclohexanol, 3-n-propylcyclohexanol, 4-n-propylcyclohexanol, 2-isopropylcyclohexanol, 3-isopropylcyclohexanol, 4-isopropylcyclohexanol, 2-n-butylcyclohexanol, 3-n-butylcyclohexanol, 4-n-butylcyclohexanol, 2-isobutylcyclohexanol, 3-isobutylcyclohexanol, 4-isobutylcyclohexanol, 2-sec-butylcyclohexanol, 3-sec-butylcyclohexanol, 4-sec-butylcyclohexanol, 2-tert-butylcyclohexanol, 3-tert-butylcyclohexanol, 4-tert-butylcyclohexanol; cycloheptanol, 2-methylcycloheptanol, 3-methylcycloheptanol, 4-methylcycloheptanol, 2-ethylcycloheptanol, 3-ethylcycloheptanol, 4-ethylcycloheptanol, 2-n-propylcycloheptanol, 3-n-propylcycloheptanol, 4-n-propylcycloheptanol, 2-isopropylcycloheptanol, 3-isopropylcycloheptanol, 4-isopropylcycloheptanol, 2-n-butylcycloheptanol, 3-n-butylcycloheptanol, 4-n-butylcycloheptanol, 2-isobutylcycloheptanol, 3-isobutylcycloheptanol, 4-isobutylcycloheptanol, 2-sec-butylcycloheptanol, 3-sec-butylcycloheptanol, 4-sec-butylcycloheptanol, 2-tert-butylcycloheptanol, 3-tert-butylcycloheptanol, 4-tert-butylcycloheptanol; cyclooctanol, 2-methylcyclooctanol, 3-methylcyclooctanol, 4-methylcyclooctanol, 5-methylcyclooctanol, 2-ethylcyclooctanol, 3-ethylcyclooctanol, 4-ethylcyclooctanol, 5-ethylcyclooctanol, 2-n-propylcyclooctanol, 3-n-propylcyclooctanol, 4-n-propylcyclooctanol, 5-n-propylcyclooctanol, 2-isopropylcyclooctanol, 3-isopropylcyclooctanol, 4-isopropylcyclooctanol, 5-isopropylcyclooctanol, 2-n-butylcyclooctanol, 3-n-butylcyclooctanol, 4-n-butylcyclooctanol, 5-n-butylcyclooctanol, 2-isobutylcyclooctanol, 3-isobutylcyclooctanol, 4-isobutylcyclooctanol, 5-isobutylcyclooctanol, 2-sec-butylcyclooctanol, 3-sec-butylcyclooctanol, 4-sec-butylcyclooctanol, 5-sec-butylcyclooctanol, 2-tert-butylcyclooctanol, 3-tert-butylcyclooctanol, 4-tert-butylcyclooctanol, 5-tert-butylcyclooctanol; decahydro-1-naphthol,

decahydro-2-naphthol, norborneol and isoborneol.

On page 15, kindly replace the first through third full paragraphs with the following:

In the step (2) of the method ~~of the present invention~~, when a solid is formed by the reaction of the primary alcohol or secondary alcohol at the reaction temperature in the step (2), the solid is used after dissolving it in the same organic solvent as the organic solvent for the step (1). The concentration of the alcohol is preferably from 0.1 to 15 mol/liter.

When the step (2) of the method ~~of the present invention~~ is carried out in the microreactor, a rearrangement reaction of the alkoxysulfonium salt shown in the formula (1) is prevented or reduced and the resulting alkoxysulfonium salt-containing liquid can be fed into the step (3).

In the step (3) of the method ~~of the present invention~~, the alkoxysulfonium salt-containing liquid is mixed with a basic compound-containing liquid and they are reacted with each other to prepare a liquid containing an aldehyde or ketone compound corresponding to the primary or secondary alcohol.

On page 16, kindly replace the second full paragraph with the following:

~~In the method of the present invention,~~ a A molar ratio of the sulfonyl compound to be supplied to step (1) to the primary or secondary alcohol to be supplied to step (2) is preferably within a range from 1:1 to 20:1, and more preferably from 1.1:1 to 3:1. When the molar ratio is less than 1:1, there may arise a problem such as left-over unreacted primary or secondary alcohol. On the other hand, when the molar ratio is more than 20:1, an operation of isolating an excess sulfonyl compound becomes complicated and there may arise industrial and economical problems.

On page 16, kindly replace the fourth full paragraph with the following:

~~In the method of the present invention,~~ a A molar ratio of the sulfonyl compound activating agent to be supplied in step (1) to the primary or secondary alcohol to be supplied in the step (2) is

preferably within a range from 1:1 to 2:1, and more preferably from 1.1:1 to 1.5:1. When the molar ratio is less than 1:1, there may arise a problem such as left-over unreacted primary or secondary alcohol. On the other hand, when the molar ratio is more than 2:1, there may arise a problem that the amount of by-products increase.

On page 17, kindly replace the first paragraph with the following:

A molar amount of the basic compound to be supplied to the step (3) of the method ~~of the present invention~~ is preferably 2 to 20 times, and more preferably 2.5 to 6 times, the molar amount of the primary or secondary alcohol. When the molar amount of the basic compound is less than 2 times as that of the primary or secondary alcohol, the efficiency of the reaction of converting of the alkoxysulfonium salt into an aldehyde or ketone may become insufficient. On the other hand, when the molar amount of the basic compound is more than 20 times as that of the primary or secondary alcohol, there may arise industrial and economical problems.

Kindly replace the paragraph spanning pages 17 and 18 with the following:

The aldehyde compound or ketone compound obtained by the method ~~of the present invention~~ corresponds to the primary alcohol or secondary alcohol used as a starting material. The following compounds can be produced by the method of the present invention:

(1) aldehydes, for example, saturated aliphatic aldehyde [for example, formaldehyde, acetaldehyde, propionaldehyde, butylaldehyde, hexanal, higher aldehyde (octaldehyde, nonaldehyde, etc.)], unsaturated aliphatic aldehyde (for example, acrolein, etc.), glyoxal, methyl glyoxal, aliphatic polyaldehyde (for example, malonaldehyde, succinaldehyde, glutaraldehyde, adipinaldehyde, pimelic aldehyde, suberinaldehyde, sebacic aldehyde, etc.), aliphatic aldehyde such as aminoacetaldehyde; aromatic aldehyde such as benzaldehyde, oxybenzaldehyde, nitrobenzaldehyde, aminobenzaldehyde, cinnamaldehyde, salicylaldehyde, anisaldehyde, 1-naphthyl-

acetoaldehyde, vanillin (vanillaldehyde), phthalaldehyde or isophthalaldehyde, terephthalaldehyde; alicyclic aldehyde such as formylcyclohexane, citronellal or citral; heterocyclic aldehyde such as nicotinaldehyde or furfural; and

(2) ketones, for example, aliphatic ketone such as acetone, methyl ethyl ketone, diethyl ketone, dipropyl ketone, methyl propyl ketone, methyl butyl ketone or pinacolone; alicyclic ketone (cyclic ketone) such as cyclopentanone, cyclohexanone, cyclooctanone, 2-methylcyclohexanone, 2-ethylcyclohexanone, 2,6-dimethylcyclohexanone, 4-chlorocyclohexanone, 4-methoxycyclohexanone, menthone or camphor; aromatic ketone such as acetophenone, propiophenone, benzophenone, deoxybenzoin or 1-naphthalenone; and heterocyclic ketone such as inden-1-one, 1,2,3-indanetrione, fluoren-9-one or 4-pyranone.

On page 18, kindly replace the second and third full paragraphs with the following:

EXAMPLES

The method ~~of the present invention~~ will now be described in more detail by way of the following examples.

Example 1

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 20, kindly replace the third full paragraph with the following:

Example 2

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 23, kindly replace the first paragraph with the following:

Example 3

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 27, kindly replace the third full paragraph with the following:

Example 5

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 29, kindly replace the third full paragraph with the following:

Example 6

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

Kindly replace the paragraph spanning pages 31 and 32 with the following:

Example 7

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactors.

On page 34, kindly replace the second full paragraph with the following:

Example 8

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the reactors shown below.

On page 36, kindly replace the third full paragraph with the following:

Example 9

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactors.

On page 38, kindly replace the third full paragraph with the following:

Example 10

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactors.

On page 41, kindly replace the first full paragraph with the following:

Example 11

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactors.

On page 43, kindly replace the third full paragraph with the following:

Example 12

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 45, kindly replace the third full paragraph with the following:

Example 13

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 47, kindly replace the third full paragraph with the following:

Example 14

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 50, kindly replace the first full paragraph with the following:

Example 15

In the production of decanal from decanol by the method ~~of the present invention~~, the steps

(1), (2) and (3) were carried out using the following reactor.

On page 52, kindly replace the third paragraph with the following:

Example 16

In the production of 2-octanone from 2-octanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactors.

On page 54, kindly replace the third full paragraph with the following:

Example 17

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactors.

On page 56, kindly replace the third full paragraph with the following:

Example 18

In the production of benzaldehyde from benzyl alcohol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 59, kindly replace the first full paragraph with the following:

Example 19

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out by using the following reactors.

On page 61, kindly replace the third full paragraph with the following:

Example 20

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out by using the following reactor.

On page 63, kindly replace the third full paragraph with the following:

Example 21

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out by using the following reactor.

On page 65, kindly replace the third full paragraph with the following:

Example 22

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 68, kindly replace the first full paragraph with the following:

Example 23

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 70, kindly replace the first full paragraph with the following:

Example 24

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 72, kindly replace the first full paragraph with the following:

Example 25

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 74, kindly replace the first full paragraph with the following:

Example 26

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 76, kindly replace the first full paragraph with the following:

Example 27

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 78, kindly replace the first full paragraph with the following:

Example 28

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 80, kindly replace the first full paragraph with the following:

Example 29

In the production of cyclohexanone from cyclohexanol by the method ~~of the present invention~~, the steps (1), (2) and (3) were carried out using the following reactor.

On page 82, kindly replace the first full paragraph with the following:

Example 30

In the production of cyclohexanone from cyclohexanol by the method of the present invention, the steps (1), (2) and (3) were carried out using the following reactor.

On page 108, kindly replace the first full paragraph with the following:

INDUSTRIAL APPLICABILITY

~~The~~Our methods ~~of the present invention~~ enables the production of a aldehyde or ketone compound from a corresponding primary alcohol or secondary alcohol at a comparatively high temperature, compared to the low temperature of -30°C or lower in a conventional method, within a short time and with a high yield. Therefore it is practically useful.

In the Claims

1. (Currently Amended) A method for producing an aldehyde or ketone compound by using a microreactor, comprising ~~a step (1) of~~ mixing a liquid containing a sulfoxide compound with a liquid containing an activating agent for the sulfoxide compound to ~~allow them to react to~~ cause a reaction with each other and to produce an activation reaction product of the sulfoxide compound; a ~~step (2) of~~ mixing ~~the~~ a liquid containing the activation reaction product of the sulfoxide compound with a liquid containing at least one member selected from primary and secondary alkyl alcohols to ~~allow them to react to~~ cause a reaction with each other and to prepare a liquid containing an alkoxysulfonium salt; and ~~a step (3) of~~ mixing the resulting liquid containing an alkoxysulfonium salt with a basic compound-containing liquid to ~~allow them to react to~~ cause a reaction with each other and to prepare a liquid containing an aldehyde or ketone compound corresponding to the alkyl alcohol, wherein at least one ~~step of~~ steps (1), (2) and (3) is carried out by using a microreactor.
2. (Original) The method according to claim 1, wherein the microreactor comprises two liquid-introducing channels having a fine cross-sectional profile for introducing two type of liquids; one micromixer portion for mixing and reacting two kinds of liquids introduced, with each other having a fine cross-sectional profile and connected to the liquid introducing channel; and one liquid discharging channel for discharging a reaction product liquid from the micromixer portion, having a fine cross-sectional profile.
3. (Original) The method according to claim 2, wherein two steps connected to each other are carried out by using a microreactor and a liquid discharging channel of a reactor of an upstream step and a liquid introducing channel of a reactor of a downstream step connected to the upstream step, are connected with each other through a connecting capillary tube.

4. (Currently Amended) The method according to claim 1 ~~or 2~~, wherein ~~the steps (1) and (2)~~ are carried out in the microreactor.

5. (Currently Amended) The method according to ~~any one of claims 2 to 4~~, wherein the temperature of the liquids in the micromixer portion and the liquid discharging channel of the microreactor is adjusted to a desired value.

6. (Original) The method according to claim 3, wherein the temperature of the liquids in the connecting capillary tube is adjusted to a desired value.

7. (Currently Amended) The method according to ~~any one of claims 2 to 6~~, wherein the cross-sectional area of the liquid introducing channel, that of the liquid micromixer portion and that of the liquid discharging channel in the microreactor, are, respectively, about $0.7\ \mu\text{m}^2$ to about $1\ \text{mm}^2$, about $0.7\ \mu\text{m}^2$ to about $1\ \text{mm}^2$ and about $0.7\ \mu\text{m}^2$ to about $1\ \text{mm}^2$.

8. (Currently Amended) The method according to ~~any one of claims 2 to 7~~, wherein a major diameter/minor diameter ratio of the cross section of the liquid introducing channel, the liquid micromixer portion and the liquid discharging channel in the microreactor, is 1 or more and the minor diameter is within a range from about $1\ \mu\text{m}$ to about $1\ \text{mm}$.

9. (Currently Amended) The method according to ~~any one of claims 1 to 8~~, wherein, in the microreactor, the flow rate of the liquid to be discharged from the liquid micromixer is adjusted so that two kinds of liquids mixed with each other can be reacted to each other in the microreactor with a desired mixing efficiency and a desired retention time.

10. (Currently Amended) The method according to ~~any one of claims 1 to 9~~, wherein the residence time of the liquid in the microreactor is adjusted to within a range from about 0.001 to about 60 seconds.

11. (Currently Amended) The method according to claim 2, wherein ~~the step~~(1) is carried out using a microreactor and the residence time of a mixed reaction solution of the sulfoxide compound-containing liquid with an activating agent-containing liquid in a portion of the microreactor between the inlet of the micromixer portion and the inlet of the reactor for ~~the step~~(2) is in the range of from about 0.001 to about 60 seconds.

12. (Currently Amended) The method according to claims 1 ~~to 11~~, wherein ~~the step~~(1) is carried out in the microreactor and the reaction temperature in ~~the step~~(1) is in the range of from about -80 to about +50°C.

13. (Currently Amended) The method according to ~~any one of~~ claims 1 ~~to 11~~, wherein ~~the step~~(2) is carried out in the microreactor and the mixing reaction temperature in ~~the step~~(2) is in the range of from about -80 to about +50°C.

14. (Currently Amended) The method according to ~~any one of~~ claims 1 ~~to 13~~, wherein the sulfoxide compound is selected from a dialkyl sulfoxide.

15. (Original) The method according to claim 14, wherein dimethyl sulfoxide is used as the dialkyl sulfoxide.

16. (Currently Amended) The method according to ~~any one of~~ claims 1 ~~to 13~~, wherein the activating agent for a sulfoxide compound is selected from the group consisting of acetic anhydride, oxalyl chloride, trifluoroacetic anhydride, trifluoromethanesulfonic anhydride, diphosphorus pentoxide, chlorine, benzoyl chloride, acetyl chloride, methanesulfonyl chloride, p-toluenesulfonyl chloride, sulfur trioxide-pyridine complex and 2,4,6-trichloro-1,3,5-triazine.

17. (Currently Amended) The method according to ~~any one of~~ claims 1 ~~to 16~~, wherein the primary and secondary alcohols are selected from saturated and unsaturated C₁-C₂₀ aliphatic primary and secondary alcohols, or saturated and unsaturated aliphatic primary and secondary alcohols

having an alicyclic aromatic hydrocarbon group, and saturated and unsaturated primary and secondary alcohols having a heterocyclic group.

18. (Currently Amended) The method according to ~~any one of claims 1 to 17~~, wherein the basic compound is selected from organic amine compounds.

19. (Original) The method according to claim 18, wherein the organic amine compound is selected from trialkylamines.

20. (Currently Amended) The method according to ~~any one of claims 1 to 19~~, wherein a molar ratio of the sulfoxide compound to be supplied ~~to the first step in (1)~~ to the primary or secondary alcohol to be supplied ~~to the second step in (2)~~ is within a range of from 1:1 to 20:1.

21. (Currently Amended) The method according to ~~any one of claims 1 to 20~~, wherein a molar ratio of the activating agent for a sulfoxide compound to be supplied ~~to the first step in (1)~~ to the primary or secondary alcohol to be supplied ~~to the second step in (2)~~ is within a range of from 1:1 to 2:1.

22. (Currently Amended) The method according to ~~any one of claims 1 to 21~~, wherein a molar amount of the base compound to be supplied ~~to the third step in (3)~~ is 2 to 20 times the molar amount of the primary or secondary alcohol to be supplied ~~to the second step in (2)~~.

23. (Currently Amended) The method according to ~~any one of claims 1 to 22~~, further comprising ~~a step of~~ isolating the target aldehyde or ketone compound from the aldehyde or ketone compound-containing liquid prepared in ~~the step (3)~~.